



Published in final edited form as:

Orbit. 2022 December ; 41(6): 739–744. doi:10.1080/01676830.2021.2012205.

Social determinants associated with loss of an eye in the United States using the *All of Us* nationwide database

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Abstract

Purpose: To identify common factors associated with the loss of an eye using the NIH *All of Us* (“*All of Us*”) database, a nationwide data repository with diverse participant enrollment.

Methods: In this case-control study, we extracted electronic health record and socio-demographic data for 231 cases of eye loss (e.g. status post enucleation, evisceration, enucleation, or diagnosis code related to anophthalmos) derived from *All of Us* enrollment sites nationally. Controls (N=924) were selected to have demographic characteristics matching the 2020 United States Census. Bivariate analyses and multivariable logistic regression identified medical and social determinants significantly associated with increased odds of losing an eye. Statistical significance was defined by $p < 0.05$.

Outcome measures: Medical and social determinants associated with increased odds of losing an eye

Results: Among cases, the average age (standard deviation) was 60.1 (14.4) years. The majority (125, 54.1%) were male. 87 (37.7%) identified as African American, and 49 (21.2%) identified as Hispanic or Latino. Loss of an eye was more likely in those with ocular tumor (odds ratio [OR] 421.73, 95% confidence interval [CI] 129.81-1959.80, $p < 0.001$), trauma (OR 13.38, 95% CI 6.64-27.43, $p < 0.001$), infection (OR 11.46, 95% CI 4.11-32.26, $p = 0.001$) or glaucoma (OR 8.33, 95% CI 4.43-15.81, $p < 0.001$). African American (OR 2.39, 95% CI 1.39-4.09, $p = 0.002$) and Hispanic or Latino (OR 1.80, 95% CI 1.01-3.15, $p = 0.04$) participants were disproportionately affected.

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Disclosure of interest

There are no conflicts of interest to declare.

Conclusions: Racial and ethnic disparities exist among those with loss of an eye from various underlying conditions. Efforts addressing health inequities may mitigate the risk of this morbid outcome.

Keywords

loss of eye; enucleation; health inequities; big data; social determinants of health

Introduction

Evisceration, enucleation, and exenteration are regarded as end-stage treatment for conditions such as ocular trauma, ocular tumors, and severe endophthalmitis. The resulting loss of an eye can have detrimental effects on a patients' quality of life. In addition to aesthetic disfigurement, lack of stereopsis can limit independent activities of daily life. Even with an ocular prosthesis, patients report higher levels of anxiety and depression after enucleation, and often require additional procedures for anophthalmic-related orbital changes that occur over time.^{1,2} Major ophthalmic risk factors leading to the loss of eye include endophthalmitis, trauma, and intraocular tumor.³ Inequalities in social determinants of health are closely linked to these risk factors; for instance, studies in other countries have demonstrated that increasing socioeconomic deprivation is associated with increasing frequency of serious ocular trauma.⁴ Within the United States, the socio-demographic determinants associated with loss of an eye have not been well characterized.

The *All of Us* Research Program ("*All of Us*"), launched in May 2018, is an unprecedented effort by the National Institutes of Health to collect and study data from 1 million adult participants across the United States. *All of Us* prioritizes the enrollment of underrepresented minorities in order to reflect the increasing diversity of the United States.^{5,6} To date, the database offers electronic health record (EHR) and survey data for more than 368,000 adult participants from various enrollment sites, and enrollment is ongoing.⁷ There are numerous domains of EHR data, including labs and measurements, procedures, conditions, and drug exposures; however, individual patient medical records and clinical notes are not available. This case-control study utilizes the diversity and scale of the *All of Us* database to identify patterns of health disparities associated with increased odds of losing an eye. To validate the data from the *All of Us* database, medical risk factors for the loss of eye were identified and compared to previously reported risk factors. Given the limitations of the loss of an eye on functionality and quality of life, identifying and addressing these disparities can inform strategies to improve equality in access to care and reduce the risk of adverse outcomes.

Methods

All of Us is a database including surveys, electronic health record data, and physical measurements. EHR data regarding medical conditions, procedures, and labs and measurements are linked for all consented participants. Upon enrollment, participants complete a basic demographic survey which assesses factors like education level, household income, and employment status. The full survey is available online.⁸

HIPAA compliance is maintained in the *All of Us* database as all data have been transformed and de-identified across each participant record to protect participant privacy. These transformations include: data suppression of codes with a high risk of identification, generalization of categories such as age, sex at birth, gender identity, sexual orientation, and race. The *All of Us* Registered Tier Curated Data Repository Data Dictionary contains formal documentation on privacy implementation and creation of the data repository.¹¹ Secondary analyses of de-identified data included in *All of Us*, such as that presented here, are considered non-human subjects research. Data collection was approved by the *All of Us* Institutional Review Board and adhered to the Declaration of Helsinki.

At the time of analysis on June 2021, there were 314,277 adult participants enrolled in *All of Us*. Cases were defined by adult (age 18 years and above) participants with qualifying International Classification of Diseases (ICD) and Systematized Nomenclature of Medicine (SNOMED) condition codes as well as Current Procedure Terminology (CPT) procedure codes. Qualifying conditions included anophthalmos and phthisis bulbi, and qualifying procedures included enucleation, evisceration, and exenteration (see Supplemental Table 1 for complete list of qualifying codes).

There were a total of 231 cases of eye loss. Using a 4:1 control to case ratio, we generated a sample of controls (N=924) matching the 2020 United States Census with regards to gender, race, and ethnic distributions using the R package *MatchIt*.⁹ Descriptive statistics of the *All of Us* study cohort were generated (Table 1). The prevalence of loss of eye cases for each state was generated using the 2020 United States Census population data for each state.⁹ Characteristics of cases and controls were compared using chi-squared analyses for categorical variables and t-tests for continuous variables, and use of t-tests was confirmed by evaluating symmetric distributions of continuous data and verifying other assumptions required for parametric hypothesis testing. Statistical significance was defined by $p < 0.05$.

R programming was used for all logistic regression modeling. The following R packages were used: *ggplot2*, *tibble*, *tidyr*, *readr*, *purrr*, *dplyr*, *stringr*, *forcats*. Concept sets were created for each of the following predictors: ocular tumors (i.e. choroidal melanoma, malignant neoplasm of ciliary body, carcinoma in situ of eye, etc.), ocular trauma (i.e. avulsion of eye, orbital floor fracture, globe rupture, etc.), infection (i.e. endophthalmitis, chorioretinitis, vitritis, etc.), autoimmune/inflammatory conditions (i.e. sympathetic uveitis and retinal vasculitis), diabetes, and glaucoma. A complete list of qualifying diagnoses for each concept set is available in Supplemental Table 2. To establish a temporal relationship between predictors and outcome, data were included only if the predictors preceded the outcome diagnosis of loss of eye.

Correlation coefficients were generated to identify highly correlated variables. Bivariate analyses were performed to determine statistically significant variables. Bivariate (crude) odds ratios (OR) and 95% confidence intervals (CIs) were calculated for all predictors. A multivariable logistic regression model was then generated using bidirectional stepwise feature selection to identify variables significantly associated with increased odds of loss of eye. With the best-performing multivariable model, we calculated and reported adjusted odds ratios, 95% CIs, and associated p-values. Statistical significance was defined as $p < 0.05$.

All statistical analyses were performed in an R notebook within the *All of Us* Researcher Workbench environment and can be accessed in our publicly available workspace.¹⁰

Results

A total of 231 cases of loss of eye were identified (Table 1). The average age (standard deviation) of those with a history of loss of eye was 60.1 (14.4) years. The average age at which eye loss occurred was 53.3 (14.8) years, with a range from 18.8 to 87.3 years. The majority (N=125, 54.1%) were male. Over one-third of cases (87 [37.7%]) identified as African American, and over one-fifth of cases (49 [21.2%]) identified as Hispanic or Latino. This demonstrated a key racial disparity, as cases of loss of eye had a significantly higher representation of African American participants (37.3% among cases vs. 13.3% among controls, $p<0.001$). Among the cases, the majority (N=220, 95.2%) reported health insurance coverage, and the most well-represented payors were Medicaid (90 [39%]) and Medicare (92 [39.8%]). The majority (N=134, 58.0%) indicated they were renting their current home. 119 (51.2%) reported an annual income less than \$50,000. 182 (78.8%) were not currently employed, and 71 (30.7%) reported a college or advanced degree. States with the highest prevalence of eye loss (cases of loss of eye over total state population as reported by United States Census data) included: Wisconsin, Massachusetts, Illinois, New York, and Pennsylvania.

Bivariate analyses to identify predictors associated with increased odds of loss of eye demonstrated several significant medical and social variables. Medical indications included ocular tumor (OR 315.08, 95% CI 116.47-1293.52, $p<0.001$), ocular trauma (OR 17.61, 95% CI 11.22-28.40, $p<0.001$), glaucoma (OR 12.14, 95% CI 8.32-17.91, $p<0.001$) and diabetes (OR 3.21, 95% CI 2.34-4.39, $p<0.001$). Those who identified as African American (OR 3.93, 95% CI 2.84-5.46, $p<0.001$) or those renting current housing (OR 3.16, 95% CI 1.93-5.40, $p<0.001$) were associated with a higher risk of eye loss. Employment, higher annual income, and higher education level were associated with lower risk (Table 2). In our multivariable logistic regression modeling, African American (OR 2.39, 95% CI 1.39-4.09, $p=0.002$) and Hispanic or Latino ethnicity (OR 1.80, 95% CI 1.01-3.15, $p=0.04$) were significantly associated with increased odds of losing an eye even after adjusting for medical factors such as trauma, infection, glaucoma, or diabetes (Table 3).

Discussion

The permanent loss of an eye due to enucleation, evisceration, or exenteration is regarded as the end-stage outcome of many ophthalmic diseases. Early diagnosis and proper management is crucial in preventing this morbid outcome. Prior studies investigating risk factors for enucleation and evisceration were primarily conducted at single institutions outside the United States, with limited access to socio-demographic data and from several decades ago.¹¹⁻¹³ Our study utilizes a novel nationwide United States database with demographic data from a diverse population to identify several risk factors associated with increased odds of losing an eye.

Among our study cohort, the loss of an eye occurred at a mean age of 53.3 years and in males, consistent with the demographics reported in prior reviews.¹² Previous studies have also demonstrated an additional peak incidence among pediatric patients; however, the *All of Us* database is currently only open to enrollment of adult participants 18 years and above.^{13,14} Our multivariable regression model indicated several clinical causes for loss of eye, including ocular trauma, tumors, diabetes, and glaucoma. Of these, the top two most common indications were ocular tumor and trauma. This is comparable to results from prior single-center studies performed internationally in China, Turkey, and Denmark and thereby validates the data within the *All of Us* database.^{12,13,15} Studies by Setlur et al. at the Doheny Eye Institute and Günalp et al. reported a decreasing frequency of enucleation over a 20 to 60 year period, likely secondary to advancements in glaucoma management, globe-saving surgical techniques, and precision imaging.^{16,17} Despite improved diagnostic and therapeutic methods, external influences, such as social determinants of health, may explain why these trends persist even decades later.

Our multivariable regression model demonstrated that racial and ethnic disparities were independently associated with the loss of eye, even after adjusting for potential confounding social variables (e.g. education and income level). Most notably, African American and Hispanic or Latino populations are at higher risk. Studies have shown that ocular trauma is more common in African American and Hispanic adults.¹⁸ To the best of our knowledge, no studies have investigated the direct relationship between race and ethnicity and the loss of an eye from various underlying conditions. There are several possible explanations for this association, including barriers to healthcare access and implicit biases among healthcare providers. In addition, some eye diseases are more prevalent in certain populations and can result in the need for enucleation or evisceration if left untreated. For instance, African Americans are disproportionately affected by glaucoma and resulting vision loss and blindness compared to other populations in the United States.¹⁹ African Americans typically suffer from higher mean intraocular pressure levels with a predisposition for more rapid glaucoma progression.¹⁹⁻²¹ Studies have theorized that genetic or biological variations may explain this trend.²⁰

Race and ethnicity are closely intertwined with socioeconomic factors such as annual income, employment status, and educational status. These factors influence patterns in access to care, with vulnerable populations facing larger barriers to care. As an example, ocular trauma is a major risk factor for the loss of eye, as shown in both our logistic regression modeling and in previous studies.²² African American and Hispanic individuals as well as those from low socioeconomic backgrounds are most commonly affected by ocular trauma. These subgroups are more likely to work in hazardous work environments which increase their risk for occupational globe injuries.^{23,24} Delays in timely care may result from inadequate resources or financial pressures that make it difficult to take time off work. Other frequently cited barriers to health care utilization include unemployment and high costs of care.^{25,26} Our findings therefore allude to the ways in which social and economic norms may reinforce racial inequities in various domains, including healthcare.²⁷ Efforts to achieve health equity should seek to challenge the inherent inequities in access to capital that maintain racial health disparities.

The racial and ethnic disparities associated with eye loss highlight the importance of equipping physicians with tools to provide culturally sensitive care for diverse patient populations. Cultural and language differences between patients and providers may impact effective communication, especially when caring for patients with chronic conditions that require sustained patient engagement and management. Focused curriculum on providing cross-cultural care during medical training and beyond can therefore potentially improve patient outcomes and satisfaction with care.²⁸

A major strength of using the *All of Us* database is the enrollment of underrepresented minorities. This is especially relevant given that African Americans and Hispanics are historically underrepresented in ophthalmology research and clinical trials.²⁹ As a testament to the program's commitment to diversity, our initial analyses of the database revealed that 21.94% of enrolled adults identified as African American. The national scale of *All of Us* is an additional strength, as the program has multiple enrollment sites in both academic and community settings across the country. Finally, the *All of Us* database offers sociodemographic information (i.e. highest attained education level, annual income, etc.) and survey data that are not readily available in routine EHRs. Limitations of this study include the inability to establish a causal relationship due to the case-control study design. Cohort definitions relied upon diagnostic billing codes, and it is possible misclassification or inconsistencies in diagnoses occurred, although this is a limitation common to analyses of claims and EHR data. Clinical notes documenting visual acuity and the severity of injury, tumor invasion, or infection are also not currently available through the database.

Conclusion

This analysis of nationwide data demonstrates that major racial and ethnic disparities exist in conditions and procedures leading to loss of an eye. Given the extent of morbidity associated with loss of an eye, these findings highlight the need for further efforts to reduce inequities in healthcare access and address implicit biases.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding details:

This study was supported by the National Institutes of Health (Bethesda, MD, Grant 1DP5OD029610) and an unrestricted departmental grant from Research to Prevent Blindness. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH. The funders had no role in the design or conduct of this research.

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Table 1.

Demographic characteristics of adults who have lost an eye in the NIH *All of Us* research program and controls matched to the 2020 United States Census

| | Loss of eye cases (N=231) | Controls (N=924) | p-value |
|--------------------------------|---------------------------|------------------|---------|
| Mean Age (SD) in years | 60.1(14.4) | 59.7 (16.7) | 0.69 |
| Gender [N(%)] | | | |
| Male | 125(54.1) | 469(50.8) | 0.21 |
| Female | 106(45.9) | 455(49.2) | |
| Self-reported race [N(%)] | | | |
| White | 89(38.5) | 705(76.3) | <0.001 |
| Black | 87(37.7) | 123(13.3) | |
| Other | 50(21.7) | 42(4.6) | |
| Asian | <20(<5) * | 54(5.8) | |
| Self-reported ethnicity [N(%)] | | | |
| Not Hispanic or Latino | 182(78.8) | 754(81.6) | 0.38 |
| Hispanic or Latino | 49(21.2) | 170(18.4) | |

* Counts less than 20 are not shared in accordance with All of Us data reporting policies

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Table 2.

Bivariate crude odds ratios for variables significantly associated with increased odds of loss of eye

| Variable | Crude Odds Ratio | 95% Confidence Interval | p-value |
|------------------------|------------------|-------------------------|---------|
| Ocular tumor | 315.08 | 116.47-1293.52 | <0.001 |
| Ocular trauma | 17.61 | 11.22-28.40 | <0.001 |
| Ocular infection | 14.82 | 7.64-31.07 | <0.001 |
| Sympathetic ophthalmia | 13.12 | 6.50-28.73 | <0.001 |
| Glaucoma | 12.14 | 8.32-17.91 | <0.001 |
| African American | 3.93 | 2.84-5.46 | <0.001 |
| Diabetes | 3.21 | 2.34-4.39 | <0.001 |
| Renting current home | 3.16 | 1.93-5.40 | <0.001 |
| Annual income | 0.85 | 0.79-0.91 | <0.001 |
| Education level | 0.80 | 0.69-0.92 | 0.002 |
| Employed | 0.55 | 0.38-0.77 | 0.001 |

Table 3.

Multivariate odds ratios for variables significantly associated with increased odds of loss of eye

| Variable | Adjusted Odds Ratio | 95% Confidence Interval | p-value |
|------------------------------|----------------------------|--------------------------------|----------------|
| Ocular tumor | 333.16 | 108.35-1480.29 | <0.001 |
| Ocular trauma | 11.96 | 6.18-23.44 | <0.001 |
| Ocular infection | 10.06 | 3.80-26.84 | <0.001 |
| Glaucoma | 7.91 | 4.34-14.50 | <0.001 |
| African American | 2.39 | 1.39-4.09 | 0.002 |
| Diabetes | 2.07 | 1.23-3.43 | 0.005 |
| Hispanic or Latino ethnicity | 1.80 | 1.01-3.15 | 0.04 |

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